

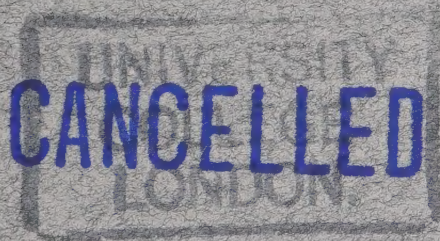
Reprinted from the American Journal of Physiology.

VOL. XXIX. — DECEMBER 1, 1911. — No. II.

EMOTIONAL GLYCOSURIA.

By W. B. CANNON, A. T. SHOHL, AND W. S. WRIGHT.

[FROM THE LABORATORY OF PHYSIOLOGY IN THE HARVARD MEDICAL SCHOOL.]



C.

WELLCOME INSTITUTE LIBRARY	
Coll.	weIMOmec
Coll.	pam
No.	WK 800
	1911
	C22e



22500892941

EMOTIONAL GLYCOSURIA.¹

By W. B. CANNON, A. T. SHOHL, AND W. S. WRIGHT.

[From the Laboratory of Physiology in the Harvard Medical School.]

IN clinical literature scattered suggestions are to be found that emotional states may be the cause of more or less permanent glycosuria. Great grief and prolonged anxiety during a momentous crisis have been regarded as causes of individual instances of diabetes, and anger or fright has been followed by an increase in the sugar excreted by persons who already have the disease.² The onset of diabetes in a man directly after his wife was discovered in adultery is described by Naunyn, and this author also cites two cases in his own practice, — one started during the bombardment of Strassburg (1870), the other started a few days after a companion had shot himself.³ In cases of mental disease, also, states of depression have been described accompanied by sugar in the urine. Schultze has reported that in these cases the amount of glycosuria is dependent on the degree of depression, and that the greatest excretion of sugar occurs in the fear-psychoses.⁴ Raimann has reported that in both melancholia and mania the assimilation limit of sugar may be lowered.⁵ And Arndt has observed glycosuria appearing and disappearing as alcoholic delirium appeared and disappeared in his patients.⁶

¹ A preliminary announcement of the results of this investigation was made at the meeting of the American Philosophical Society, Philadelphia, April 22, 1911. See Proceedings, American Philosophical Society, 1911, I, p. 227; also Science, 1911, xxxiii, p. 907.

² See KLEEN: On diabetes mellitus and glycosuria, Philadelphia, 1900, pp. 22, 37-39.

³ NAUNYN: Der Diabetes mellitus, Vienna, 1898, p. 72.

⁴ SCHULTZE: Verhandlungen der Gesellschaft deutscher Naturforscher und Ärzte, Cologne, 1908, II, p. 358.

⁵ RAIMANN: Zeitschrift für Heilkunde, 1902, xxiii, Abtheilung III, pp. 14, 19.

⁶ ARNDT: Zeitschrift für Nervenheilkunde, 1897, x, p. 436.

Although clinical evidence thus indicates an emotional origin of some cases of diabetes and glycosuria, the intricacies of existence and the complications of disease in human beings throw some doubt on the value of that evidence. Both Naunyn and Hirschfeld, although mentioning instances of diabetes apparently due to an emotional experience, urge a skeptical attitude towards such statements.⁷ It is desirable, therefore, that the question of an emotional glycosuria be tested under simpler and more controllable conditions. "Emotional glycosuria" in experimental animals has indeed been referred to by Waterman and Smit⁸ and more recently by Henderson and Underhill.⁹ Both these references, however, are based on the work of Böhm and Hoffmann, reported in 1878.¹⁰ Böhm and Hoffmann found that cats, when bound to an operating board, tracheotomized (without anæsthesia), and in some instances catheterized by a suprapubic exposure of the urethra, had in about half an hour an abundance of sugar in the urine. In three determinations sugar in the blood proved slightly above normal so long as sugar was appearing in the urine, but returned to normal as the glycosuria disappeared. Since they were able to produce the phenomenon by simply binding animals to the holder, they called it "Fesselungsdiabetes."

As possible causes of this glycosuria in bound animals, they considered tracheotomizing, cooling, and pain. The first two they readily eliminated, and still they found sugar excreted. Pain they could not obviate, and since, without binding the animals, they caused glycosuria by merely stimulating the sciatic nerves, they concluded that painful confinement was itself a sufficient cause. Other factors, however, such as cooling and circulatory disturbances, probably cooperated with pain, they believed, to produce the result.

Inasmuch as Böhm and Hoffmann did not mention the emotional element in discussing their results, and inasmuch as they admitted that they could not obviate from their experimental procedure pain, which they themselves proved was effective in causing glycosuria,

⁷ NAUNYN: *Loc. cit.*, p. 73; HIRSCHFELD, *Die Zuckerkrankheit*, Leipzig, 1902, p. 45.

⁸ WATERMAN and SMIT: *Archiv für die gesammte Physiologie*, 1908, cxxiv, p. 205.

⁹ HENDERSON and UNDERHILL: *This journal*, 1911, xxviii, p. 276.

¹⁰ BÖHM and HOFFMANN: *Archiv für experimentelle Pathologie und Pharmakologie*, 1878, viii, p. 295.

designating what they called "Fesselungsdiabetes" as "emotional glycosuria" is not justified.

The discovery that during fright (or rage?) the adrenal secretion is increased,¹¹ and the fact that injection of epinephrin gives rise to glycosuria, suggested that glycosuria might be called forth by emotional excitement, and then that even without the painful element of Böhm and Hoffmann's experiments sugar might be found in the urine.

The first procedure, in testing this suggestion, was a repetition of Böhm and Hoffmann's experiments freed from the factor of pain. The animals (cats) were bound to a comfortable holder, which left the head unfastened, and which had been used hundreds of times in X-ray studies of digestion, with many different animals, without causing any signs of even so much as uneasiness.¹² Just as in observations on the movements of the alimentary canal, however, so here the animals reacted differently to the experience of being confined. Young males usually became quite frantic, and with eyes wide, pupils dilated, pulse accelerated, hairs of the tail more or less erect, they struggled, snarling and growling, to free themselves. Females, on the contrary, especially if elderly, were as a rule much more calm, and resignedly accepted the novel situation.

According to differences in reaction the animals were left in the holder for periods varying in length from thirty minutes to five hours (see Table I). In order to insure prompt urination, considerable quantities of water were given by stomach tube at the beginning of the experiment and in some cases again later. Arrangements were made for draining the urine promptly, when the animal was on the holder or when afterwards in a metal metabolism cage, into a glass receiver containing a few drops of chloroform. The diet in all cases consisted of customary raw meat and milk. In every instance the urine was proved free from sugar before the animal was used.

In the present series of observations twelve cats were used, and in every one a well-marked glycosuria was developed. The shortest periods of confinement to the holder which were effective were thirty and forty minutes; the longest we employed, five hours. The average time required to bring about a glycosuria was less than an hour and a half; the average in seven of the twelve cases (A, C, D, E, G, H,

¹¹ CANNON and DE LA PAZ: This journal, 1911, xxviii, p. 64.

¹² CANNON: This journal, 1898, i, p. 363.

and K, Table I) was less than forty minutes. In all cases no sugar was found in the urine passed on the day after the excitement.

The promptness with which the glycosuria developed was directly related to the emotional state of the animal. Sugar was found early in animals which early showed signs of being frightened or in a rage, and much later in animals which took the experience more calmly (*cf.* E, F, and I in Table I with B, C, D, J, and K).

As cooling may result in hyperglycæmia, and consequent glycosuria, the rectal temperature was observed from time to time, and it was found to vary so slightly that, as far as these experiments might be concerned, it was a wholly negligible factor. In cat G the rectal temperature fell to 36° C. while the animal was bound and placed in a cold room (about 2° C.) for fifty minutes, but no sugar appeared in the urine.

Further evidence that the appearance of sugar in the urine may arise purely from emotional excitement was obtained from three cats (A, G, and H, Table I) which gave negative results when bound in the holder for varying periods up to four hours. It was noteworthy that these animals remained calm and passive in their confinement. When, however, they were placed separately in a small wire cage, and were barked at by an energetic little dog, that jumped at them and made signs of attack, the cats became much excited, they showed their teeth, humped their backs, and growled defiance. This sham fight was permitted to continue for a half-hour in each of the three cases. In each case the animal, which after four hours of bondage had exhibited no glycosuria, now had sugar in the urine. Pain, cooling, and bondage were not factors in these experiments, nor in the experiment in which cat E was barked at by the dog (see Table I). The animal was either frightened or enraged by the barking dog, and that excitement was attended by glycosuria.

The sugar excreted in the twenty-four hours which included the period of excitement was determined by the Bertrand method.¹³ It ranged from 0.024 gm. to 1.93 gm., or from 8 mgm. to 0.62 gm. per kilo body weight, for the twenty-four-hour quantity.

Twenty-five samples of urine from the observed cats, twelve of the

¹³ See ABDERHALDEN: *Handbuch der biochemischen Arbeitsmethoden*, Berlin, 1910, ii, p. 181.

TABLE I.

A SUMMARY OF THE CONDITIONS OF EMOTIONAL GLYCOSURIA AND THE AMOUNTS OF SUGAR EXCRETED.

Cat.	Sex.	Experience.	Remarks.	Urine 24 hrs.	Sugar excreted 24 hrs.	Sugar per kilo body wt.
				c.c.	gm.	gm.
A	Male	Bound 1½ hrs.	Calm	400	0.0	0.0
A	Male	Bound 2 hrs.	Calm	370	0.0	0.0
A	Male	Bound 4 hrs.	Calm	150	0.0	0.0
A	Male	Dog ½ hr.	Frightened	400	0.49	0.14
B	Male	Bound 1¾ hrs.	Excited	255	1.19	0.44
C	Male	Bound ⅔ hr.	Excited	250	0.34	0.12
D	Female	Bound ⅔ hr.	Excited	140	0.69	0.38
E	Female	Bound 1 hr.	Calm	220	0.0	0.0
E	Female	Bound 2 hrs.	Calm	185	0.0	0.0
E	Female	Bound 4 hrs.	Excited	358	1.93	0.62
E	Female	Dog ¾ hr.	Excited	90	1.10	0.35
F	Male	Bound 1½ hrs.	Calm	140	0.0	0.0
F	Male	Bound 1½ hrs.	Trembled	70	0.0	0.0
F	Male	Bound 4 hrs.	Fairly quiet	240	0.035	0.015
G	Male	Dog ½ hr.	Frightened	160	0.59	0.20
G	Male	Bound 2 hrs.	Calm	340	0.0	0.0
G	Male	Bound ⅝ hr., cold room	Rect. temp. 36	90	0.0	0.0
G	Male	Bound 4 hrs.	Calm	205	0.0	0.0
H	Male	Bound 2 hrs.	Slightly excited	160	0.0	0.0
H	Male	Bound 4 hrs.	Calm	115	0.0	0.0
H	Male	Dog ½ hr.	Frightened	65	0.024	0.008
I	Female	Bound 3 hrs.	Calm	155	0.0	0.0
I	Female	Bound 5 hrs.	Cried; struggled	130	0.55	0.25
J	Female	Bound 1¼ hrs.	Cried; struggled	215	0.78	0.31
K	Female	Bound 1 hr.	Raging	95	+	...
L	Male	Bound 1 hr.	Calm	...	0.0	0.0
L	Male	Bound 1¼ hrs.	Raging	...	+	...

samples containing sugar, were tested for acetone by Legal's sodium nitro-prusside method, but were found negative.

To what extent the observations here recorded on cats will prove true for other animals used for experimentation remains to be investigated. Fischer has reported that he bound rabbits to a holder for periods lasting from twenty-four to thirty-six hours without causing sugar to appear in the urine.¹⁴ Rabbits, however, often seem to be stupefied rather than excited by this confinement. Gib has given an account of a bitch that became much agitated when shut up, and after such enforced seclusion, but never otherwise, excreted small quantities of glucose in the urine.¹⁵ Further observations on the urine of experimental animals in states of excitement are desirable.

Since splanchnic stimulation produces glycosuria,¹⁶ and since major emotions, such as rage and fright, are attended by nervous discharges along splanchnic pathways, glycosuria as an accompaniment of emotional excitement might be expected to occur. To what extent the adrenal glands which, as already mentioned, are stimulated to increased secretion by excitement, might play a part in this process, is still in dispute. Adrenalectomy or denervation of the adrenals, according to some observers,¹⁷ prevents glycosuria after puncture of the fourth ventricle, and also after stimulation of the splanchnic nerves.¹⁸ On the other hand Wertheimer and Battez state that removal of the adrenal capsules does not abolish the effects of piqure in the cat.¹⁹ It was questionable, therefore, whether removal of the adrenal glands would affect emotional glycosuria.

Evidence on this point was secured in observations on three animals that were decapsulated aseptically under ether. The animals selected (C, K, and L, Table I) had all become quickly excited on being bound

¹⁴ FISCHER: *Archiv für die gesammte Physiologie*, 1905, cix, p. 13.

¹⁵ Cited by KLEEN: *Loc. cit.*, p. 37.

¹⁶ See MACLEOD: *This journal*, 1907, xix, p. 405, also for other references to literature.

¹⁷ See MEYER: *Comptes rendus de la Société de Biologie*, 1906, lviii, p. 1123; NISHI, *Archiv für experimentelle Pathologie und Pharmakologie*, 1909, lxi, p. 416.

¹⁸ GAUTRELET and THOMAS: *Comptes rendus de la Société de Biologie*, 1909, lxvii, p. 233; and MACLEOD: *Proceedings of the Society for Experimental Biology and Medicine*, 1911, viii, p. 110 (true for left capsule and left splanchnic).

¹⁹ WERTHEIMER and BATTEZ: *Archives internationales de physiologie*, 1910, ix, p. 392.

to the holder, and had manifested glycosuria in about an hour of confinement. After opening the abdomen the adrenal veins were first tied, and then the capsules freed from their attachments and removed as quickly and with as little handling as possible. In cat K the entire operation was finished in twenty minutes. In cats K and L a small catheter was introduced into the urethra through an incision, so that the bladder could be emptied at any time.

In all three cases urine was obtained soon after the operation that was free from sugar. Although the decapsulated animals manifested a general lessening of muscular tone, they still displayed much of their former rage or excitement when bound. Indeed cat L was more excited after decapsulation than before. That the animals might not be excessively cooled they were kept warm with coverings or an electric heating pad. Although they were now bound for periods from two to three times as long as the periods required formerly to cause glycosuria, no trace of sugar was found in the urine in any instance. The evidence thus secured tends, therefore, to support the view that the adrenal glands perform an important rôle in the glycosuria resulting from splanchnic stimulation.

The question arises at this point as to the interpretation of the results reported by Böhm and Hoffmann in their paper on "Fesselungsdiabetes." Possibly the emotional element was in part accountable for the glycosuria which they observed, but the pain which they produced, as they themselves recognized, would reasonably explain it. Strong stimulation of sensory fibres will cause discharges along the splanchnic nerves, and incidentally will bring about an increased secretion of the adrenal glands.²⁰ In glycosuria resulting from painful stimulation, therefore, as well as in emotional glycosuria, the adrenal glands may be essential factors.

There is little doubt that the glycosuria following emotional excitement, like that resulting from pain, is dependent on a state of hyperglycæmia. Conceivably such hyperglycæmia may be useful to the organism. MacDougall, in associating instincts and emotions, has put together "flight instinct" and "fear emotion," and "pugnacity instinct" and "anger emotion."²¹ Both the fear emotion and the anger emotion are, in wild life, likely to be followed by activity re-

²⁰ CANNON and HOSKINS: This journal, 1911, xxix, p. 278.

²¹ MACDOUGALL: Introduction to social psychology, London, 1908, pp. 49, 59.

quiring contraction of great muscular masses in supreme and prolonged struggle. A mobilization of sugar in the blood under these circumstances might be of signal service to the laboring muscles

SUMMARY.

When cats are excited for even so short a time as one half-hour, either by being bound in a comfortable holder or by being caged and barked at by an active dog, they exhibit glycosuria. Neither pain, cooling, nor being bound, therefore, need be a factor in the result — the fright or the rage of the animal is the essential element.

The amount of sugar per kilo of body-weight, found in the urine during the twenty-four hours which included the excitement, averaged 0.26 gm. with a maximum of 0.62 gm.

Animals which had glycosuria when bound for about an hour failed to have it after careful adrenalectomy, although bound between two and three times as long as before, and still manifesting the excitement which they had manifested previous to the operation.

On the reasonable assumption that the emotional glycosuria here described is due to hyperglycæmia, a possible utility of the sugar mobilization in the blood is suggested.

THE UNIVERSITY PRESS, CAMBRIDGE, U.S. A.